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Children's anthropometrics and later disease incidence

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Abstract: Anthropometric measures in childhood predict the risk of metabolic diseases decades later. Low birth weight and short stature are associated with higher incidence of cardiovascular diseases and type 2 diabetes in adulthood supporting a hypothesis that early malnutrition has long-lasting adverse effects on metabolism. For example, low birth weight is associated with 20% increase in the risk of coronary heart disease. However, in industrialized countries over nutrition has replaced under nutrition as a major childhood risk factor of metabolic diseases. Subsequently body mass index is currently the most important anthropometric indicator in childhood predicting the risk of metabolic diseases in adulthood. One unit increase of body mass index at 13 years of age was found to increase the risk of coronary heart disease by 20%. Rapid growth in height in infancy, mid-childhood and at the start of puberty is also associated with higher risk of coronary heart disease. Physical development over childhood is closely related to nutrition and other environmental factors. Thus these associations also indicate the importance of good childhood environment for healthy adulthood.

Key words: childhood, anthropometrics, metabolism, cardio-vascular diseases, type 2 diabetes, height, BMI, birth weight

Introduction

Childhood is an important phase of life for the formation of the health risk profile in adulthood. Addressing poor health conditions and inculcating good health habits in childhood can play an important role in the prevention of adult diseases. Identifying factors in childhood affecting further

health offers measures to improve population health. Inexpensive health interventions, for example through lunches and physical exercise education, are feasible in schools and kindergarten. Many of the health habits affecting further risk of diseases are formed in childhood, and childhood is considered an important period of life for the prevention of obesity in adulthood (Baird et al. 2005). Poor childhood living conditions, such as inadequate nutrition, may also affect future health risks. Because childhood environment is difficult to measure directly, anthropometric measures in childhood and adulthood give important information on material environment reflecting childhood nutrition and other environmental conditions. When under nutrition is prevalent in a population, short stature indicates poor childhood nutrition leading also to poorer health and general frailty. This can be seen even in modern societies indicated in Figure 1. The height difference between children who grew up in the two Koreas reaches an apex at age 7 when North Korean children were, on average, about 10 cm shorter than South Korean children at the same age (Schwekendiek 2009). Those North Korean children experienced the severe famine in the mid-1990s (Haggard and Noland 2007), and thus the shorter stature indicates severe under nutrition.

(Figure 1 about here)

Within wealthy societies, there are no more groups suffering severe under nutrition. However, the dark side of this beneficial development is increased over-nutrition, leading to the increasing prevalence of obesity. Severe childhood obesity may predispose to type 2 diabetes (T2D) starting already in adolescence (Sinha et al. 2002), but even slight overweight in childhood is hazardous to health because overweight children have a high probability to become obese adults (Baird et al. 2005). Obesity in adulthood is one of the main risk factors of many chronic diseases, such as coronary heart disease (CHD) and T2D (Haslam and James 2005). Thus, body mass index (BMI, kg/m^2) has replaced height as the most important childhood anthropometric indicator of further health problems in industrialized societies.

Abnormal growth patterns in height can indicate immediate health problems as well as problems in the material conditions at home. Many chronic diseases have deep roots in childhood and thus emphasize the importance of optimal living conditions of children for the further health of population (Lozano et al. 2012). Most studies on childhood anthropometrics have examined metabolic diseases, especially CHD but also stroke and T2D. These diseases have important public health value because stroke and CHD are the leading causes of death in industrialized countries and they are also increasingly important causes of death in many developing countries; T2D incidence has also strongly increased in the world in the last two decades and it is not only an important cause of death by itself but also increases strongly the risk of CHD (Lozano et al. 2012). In this chapter the associations between cross-sectional anthropometric measures and risk of metabolic diseases is first discussed. After that results on the role of developmental trajectories in childhood in the formation of the disease risk is shown.

Cross-sectional measures

Studies using cross-sectional anthropometric measures and information on later disease incidence provide considerable insights into the role of childhood body morphology in the formation of future disease risk. In most of these studies, the baseline data are collected for reasons other than scientific purposes and decades later merged to data on chronic diseases. This sets certain limitations for research, and in most of the studies only the most basic anthropometric measures are available. However in spite of these limitations, these studies give evidence on how body morphology at a certain age predicts health risks in adulthood. They are thus important when studying the role of childhood nutrition and other environmental factors in the formation of the risk profile of metabolic diseases later in life.

Birth weight

Birth weight is the most important indicator of fetal nutrition and other environmental conditions in the uterus, since only rarely are direct measures on fetal growth available. Birth weight is a more

widely used indicator than birth length in epidemiological studies needing large sample sizes since it is much easier to measure reliably. Low birth weight can be caused by intra-uterine growth restrictions, prematurity or mother's use of toxins such as alcohol, drugs, or cigarettes (Valero De Bernabe et al. 2004). Thus birth weight can refer to actual weight at birth or it can be calculated according to the gestational age. However most of the epidemiological studies have focused only on absolute birth weight. This is at least partly because the follow-up period of several decades is needed to study chronic diseases, and reliable information on gestational age is not always available in these old baseline data sets.

The association between low birth weight and increased risk of cardio-vascular diseases (CVD) has been known for decades. One of the first researchers paying attention to this association was a British epidemiologist, David Barker, who found that weight at one year of age was inversely associated with increased CHD mortality in the UK (Barker et al. 1989). These observations contributed to his theory of biological programming, which suggests that children exposed to under nutrition in the uterus but experienced good nutrition later in life are especially predisposed to metabolic diseases in adulthood (Barker 1998). The association between birth weight and increased risk of CVD and its main physiological risk factors, such as hypertension, are well demonstrated in several longitudinal studies. In a large meta-analysis of nearly 200,000 participants, an inverse association was found between birth weight and systolic blood pressure in adulthood (Gamborg et al. 2007). Low birth weight has also been found to be consistently associated with higher CHD incidence in a review of 23 studies; in the pooled meta-analyses, low birth weight was found to be associated with 20% higher incidence of CHD (Wang et al. 2014). For stroke the studies are rarer, but there is clear evidence that low birth weight increases also the risk of stroke (Lawlor et al. 2005). An association has also been found between birth weight and T2D. In a meta-analysis of 31 studies, increase in birth weight by one kg was associated with 25% decreased risk of T2D.

(Whincup et al. 2008). Epidemiological studies thus suggest that low birth weight is consistently associated with higher risk of all metabolic diseases.

When considering the physiological background of these associations, it is important to note that there are a number of factors affecting fetal growth and future disease risk in addition to fetal nutrition. The study of twins offers an interesting opportunity to test the causal associations. It is well known that twin pregnancies are characterized by lower birth weight compared to singleton pregnancies (Buckler and Green 2004) which should thus predispose them to the higher risk of future metabolic diseases. However, previous studies have shown that both CVD (Oberg et al. 2012) and T2D risks (Petersen et al. 2011) are similar in twins and singletons. This shows that the low birth weight in twins is not a similar risk factor for future risk of these diseases as it is in singletons. There are two possible explanations for this discrepancy between twin and low-birth-weight singleton pregnancies when predicting the risk of metabolic diseases in adulthood. First, it is possible that in singletons the association between low birth weight and further disease risk is affected by confounding factors, such as low socio-economic position of mother and maternal smoking, which are associated with lower birth weight (Valero De Bernabe et al. 2004). These factors may directly or indirectly increase the lifetime risk of metabolic diseases of the newborn. Second, the developmental trajectories of fetus in twin pregnancies differ both from normal and low-birth-weight singleton pregnancies (Muhlhausler et al. 2011). So it is possible that intra-uterine environmental factors associated with restricted fetal growth patterns in singleton pregnancies predispose to further metabolic diseases, but the same does not apply to the factors affecting lower birth weight in twin pregnancies.

The latter hypothesis is supported by a study showing that in dizygotic co-twins discordant for birth weight, the lighter twin showed a higher risk of CVD (Öberg et al. 2011). Because co-twins share the same post-natal environment, this result suggests that the association is caused by fetal environmental factors. Prenatal environment may differ between co-twins because of vascular

differences which are common both in MZ and DZ twins. Thus, it is possible that the same factors, such as intrauterine nutrition, affecting low birth weight in singleton pregnancies affect also twin pregnancies creating differences in birth weight between co-twins and affecting CVD risk in adulthood. These factors can be independent of the factors affecting generally lower birth-weight of twins, which are not associated with further CVD risk.

This hypothesis is supported by the epidemiological evidence based on the cohorts born during and after the Dutch Hunger Winter. In the years 1943-45 the Netherlands suffered a severe famine, which ended immediately when the Allied forces liberated the area. Those persons who were exposed to the famine in early gestation had higher risk of CHD later in life; the prevalence of CHD was three times higher among those exposed to under nutrition in early gestation than in those who were not exposed prenatally. This difference was not explained by gestational age, socio-economic factors or smoking (Roseboom et al. 2000). There is also evidence of the vascular endothelial dysfunction, increased aortic stiffness and thicker aortic-intima media in low-birth-weight children, all predisposing to higher risk of CVD in adulthood (Norman 2008). Thus, there is clear evidence that growth restriction of fetus measured as lower birth weight and caused by, for example, poor fetal nutrition predisposes to changes in vascular function and later in life increased risk of CVD.

Height

Height has a special role among anthropometric indicators because it is easy to measure and does not change in adulthood except slight shrinking in old age. Height has been the most commonly measured anthropometric trait, and there is a vast body of scientific literature on biological, socio-economic and health related factors associated with height (Komlos 1998). Inadequate nutrition, especially the lack of protein, affects growth velocity. Poor nutrition during the period of very rapid growth in the first two years of life affects also adult stature (Sinclair 1989). If living conditions later improve, catch-up growth may compensate for the delay in growth but does not necessarily eliminate it. This was demonstrated in a review of studies on international adoptions, which found

rapid but not totally complete recovering of gap in height in two years after adoption as compared to the reference population (van Ijzendoorn et al. 2007). Further, catch-up growth does not necessarily eliminate the increased disease risks related to shorter stature in early childhood. Socio-economic differences in height can be found even in modern affluent societies, suggesting that not only severe malnutrition but otherwise inadequate diet or other material living conditions in childhood can affect growth and consequently stature in adulthood (Silventoinen 2003). Thus, adult height can be used as an indicator of nutritional status in childhood in modern industrialized societies. Height is more widely available than birth weight in large epidemiological data sets, and thus the associations between height and chronic diseases have attracted a lot of scientific interest in epidemiological studies.

The association between height and CHD risk has been widely studied; the first study showing this association was published in 1951 (Gertler et al. 1951). A meta-analysis of 52 studies found that short height was systematically associated with higher risk of CHD and in the shortest category CHD risk was about 50% higher than in the tallest category (Paajanen et al. 2010). Most of the studies were conducted in Caucasian populations, but a similar association was also found in a large study in South Korean population (Song et al. 2003). This suggests that the association between height and CHD risk is similar in East Asian populations notwithstanding their shorter mean stature as compared to Caucasian populations. The studies on the association between height and stroke are rarer. However, there is still clear evidence that short stature increases the risk of stroke both in East Asian (Song et al. 2003) and Caucasian populations. In a large Swedish study, this association did not differ according to the type of stroke, i.e., intracerebral haemorrhage, subarachoid haemorrhage and intracerebral infarction, and one standard deviation increase in height was associated around 10% decreased risk of these diseases (Silventoinen et al. 2009).

Studies on height in childhood and CHD risk are rarer because suitable datasets with adequate sample size and follow-up time are not widely available. However this association is likely because

height in childhood is an important predictor of height in adulthood. This issue was examined in a study of Swedish boys having longitudinal measures from birth until 18 years of age. Because the study participants were twins, it was possible to decompose the trait correlation into genetic correlation and correlation of environmental factors specific for each twin. Figure 2 presents the results of this study (panel A). The correlation of height at 1 year of age was 0.52 with adult height. The correlation increased when the children grew older, and at 4 years of age it was 0.74; from 12 to 15 years of age the correlation was somewhat lower probably as an effect of puberty since the start of pubertal growth peak varies between children independently of the final stature (Silventoinen et al. 2008).

(Figure 2 about here)

Taking into account the close association between height in childhood and final adult height, it is not surprising that in a large Danish study height at 7 years of age was inversely associated with incidence of CHD in adulthood so that taller boys and girls had lower incidence of CHD seen as hazard ratios less than one (Figure 3). However the association became weaker from 7 to nine year of age seeing as hazard ratios closing to 1: at 7 years of age 1 standard deviation increase in height was associated with 9% lower CHD risk in boys and 12% lower risk in girls whereas at 13 years of age the risk decrease was only 5% in boys and 9% in girls (Silventoinen et al. 2012a). These results suggest that the stature in childhood may be a better predictor of further disease risk than adult height because catch-up growth in later childhood may be associated with increased CHD risk. The greater heterogeneity of CHD risk among tall people in late childhood and in adulthood may be because this group includes both those who have been tall over childhood as compared to their peers and have low CHD risk as well as those who have experienced rapid growth later in childhood and have higher CHD risk. This underlines that adult height measures cannot fully replace measures in childhood when collecting information on childhood environment, and emphasizes the importance of collecting height measures at different phases of growth period.

(Figure 3 about here)

There is also evidence that short stature in adulthood is a risk factor of T2D even though there are far fewer studies on this topic than on the association between height and CHD. A review of nine studies found that height was inversely associated with T2D risk in women; in men the association in the pooled analysis was about the same as in women but because of larger confidence intervals it slightly failed to be statistically significant (Janghorbani et al. 2012). These results are not surprising since T2D and CVD share many of the same metabolic risk factors. This suggests that short stature is widely associated with adverse metabolic profile leading to metabolic diseases in adult life. Studies on the association between height in childhood and T2D in adulthood are rare. Anyway the close association between height in childhood and adulthood suggests that short children have increased risk for T2D in adulthood. Studies combining longitudinal measures of height in childhood to T2D incidence data in adulthood would be, however, needed to analyze whether this association will change over childhood as found for CHD risk.

As in the case of birth weight, it is not clear which factors are behind the association between height and metabolic diseases. Sometimes height is regarded purely as an indicator of childhood nutrition, and thus this association is interpreted to show that suboptimal nutrition in early childhood predisposes to further metabolic abnormalities (Barker 1998). However height is also associated with many other factors, such as socio-economic position, which may also explain this association (Silventoinen 2003). This issue was studied in a large study utilizing Nordic twin cohorts. The pooled analyses found that in twin pairs discordant for height the shorter co-twin had higher probability of death from CHD than the taller co-twin (Silventoinen et al. 2006). Also in a large Swedish study the associations of height with stroke and CHD were not explained by socio-economic factors (Silventoinen et al. 2009). These results suggest that that the association of height with adult CVD risk is not caused at least totally by social background or other postnatal

environmental factors affecting height and further CVD risk but are also affected by fetal environmental factors.

Relative weight

Obesity is currently one of the most important public health problems not only in affluent societies but increasingly also in developing countries (Komlos and Baur 2004). Obesity and overweight strongly increases the risk of many chronic disease including CVD and T2D (Haslam and James 2005). Childhood obesity is strongly increasing in many countries, and severe obesity in childhood can lead to impaired glucose tolerance or even T2D beginning in adolescence (Sinha et al. 2002). However the most important health consequence of childhood overweight is that it is strongly associated with obesity in adulthood. Thus relative weight in childhood is one of the key indicators of later health. It is well known that weight loss in adulthood is difficult, and thus the prevention of overweight in childhood is crucial. There is an important role for the prevention of childhood overweight in the prevention of adult obesity, especially because school environment offers a unique opportunity for health interventions.

Birth weight has been found to be associated with overweight risk in adulthood. A meta-analysis found that from 66 high quality studies 59 showed a linear association between birth weight and overweight risk in adulthood (Schellong et al. 2012). This association can be because of fetal nutrition but also because of genetic factors. Only four studies reported a U-shaped association between birth weight and adult BMI, and in general low birth weight was associated with a lower risk of overweight in adulthood. These results emphasize that the same anthropometric factor can affect to future health risks through different physiological pathways. For example, it is possible that genetic factors explain the linear association between birth weight and adult obesity but environmental factors explain the inverse association between birth weight and risk of metabolic diseases. More studies are needed to disentangle these different physiological pathways.

The association between current BMI and BMI in adulthood becomes stronger when children grow older. A Swedish longitudinal twin study found that the correlation between BMI at 1 year of age with BMI at 18 years of age was 0.32 (Figure 1, panel B); this correlation increased during aging and the correlation of BMI at 9 years of age was 0.69 with BMI at 18 years of age (Silventoinen et al. 2007). Also genetic correlations were high suggesting that largely the same set of genes affects relative weight from early childhood to adulthood. Similar results on the important role of genetic factors behind of the tracking of BMI over childhood have also been found in other twin studies, but the follow-up periods in these other studies ended before adulthood (Silventoinen and Kaprio 2009). The genes affecting BMI can modify metabolism, but it is likely that most of them are more related to behavioral factors such as eating styles predisposing to obesity (Faith et al. 2014). Thus, relative weight in childhood indicates further risk of obesity and the increased risk of subsequent metabolic diseases. However, the development of obesity can also be avoided by lifestyle changes since a major part of the genes predisposing to obesity act probably through behavior.

Taking into account that adult BMI is one of the most important risk factors of CVD and the strong relationship between childhood and adult BMI, BMI in childhood also predicts future risk of metabolic diseases. This was demonstrated in a large Danish study finding that BMI from 7 to 13 years of age was linearly associated with the risk of CHD in adulthood. The association also became stronger over this age period: at 7 years of age one unit increase of BMI increased the CHD risk by 9% and this association increased to 20% at 13 years of age (Baker et al. 2007). These results are consistent with the increasing correlation of BMI during the course of childhood with BMI in adulthood (Silventoinen et al. 2007). It is also noteworthy that the association between childhood BMI and risk of CHD was linear, and thus not only overweight children but also children with average BMI had increased risk to develop CHD as compared to lean children (Baker et al. 2007). These results clearly suggest that even mild overweight in childhood predisposes to CVD later in life and thus underline the need of early interventions to prevent overweight.

Other anthropometric measures

Height and weight are the most widely measured anthropometric indicators in childhood, but also other indicators have sometimes been used such as head circumference, chest circumference and leg length. The use of these anthropometric indicators can be important because they have different sensitivity periods and thus can give additional information on the role of environmental factors at different phases of physical development as compared to height and weight measures. However, a problem in epidemiological studies is that they need long follow-up time and there is lack of studies with detailed anthropometric measures and sufficient sample size to study the associations with future health risks. Thus much less is known how the other anthropometric indicators are associated with future health as compared with height and weight, especially when using measures in childhood needing follow-up time of several decades.

After height and weight, head circumference is the most widely measured anthropometric indicator in newborns and young children. The main reason for this interest is that enlarged head circumference can indicate hydrocephalus, a potentially fatal but treatable condition where cerebrospinal fluid is accumulated in the ventricles of the brain (Zahl and Wester 2008). The non-pathological variation of head circumference is linearly associated with cognitive performance (Heinonen et al. 2008), and abnormal growth patterns can also indicate increased risk of autism (Hazlett et al. 2005). However there is a lack of epidemiological studies of whether head circumference may be associated with metabolic or other chronic physical diseases in adulthood. A review of studies of internationally adopted children found rapid catch-up growth in height and weight but relatively small catch-up growth in head circumference even when these children had remarkable smaller head circumference as compared to the reference population (van Ijzendoorn et al. 2007). This suggests that head circumference may be more sensitive to fetal conditions and is affected less by post-natal environment than height. Thus epidemiological studies on the

associations between head circumference and risk of metabolic diseases are warranted and may give evidence on the role of fetal nutrition on the risk of these diseases.

Chest circumference of newborns has sometimes been used, especially in developing countries. This is because it has been found to be the most precise indicator of birth weight and so is a good proxy indicator where measuring birth weight is not feasible, for example because of lack of scale (Goto 2011). This conclusion was supported by a Japanese twin study which found that chest circumference was highly correlated with birth weight and a substantial part of this correlation was caused by environmental factors affecting both traits (Silventoinen et al. 2012b). In industrialized countries measuring of chest circumference is rare, and there are no previous studies of whether it is associated with risk of adult diseases. As in the case of head circumference, such studies would be warranted as they may give new evidence on the role of early nutrition behind risk of adult diseases.

In contrast to head and chest circumferences, leg length both in childhood and adulthood has attracted a lot of scientific interest in epidemiology. As in the case of height, the advantage of leg length is that it does not change in adulthood, and thus adult measures can be used as an indicator of childhood environmental conditions. During the very rapid growth period of the first two years of life, legs grow relatively faster than other parts of body (Sinclair 1989). Thus it is attractive to speculate that leg length would better capture differences in early nutrition as compared to stature. In a large Chinese study, leg length was inversely associated with CVD mortality in women but not in men. However, also in women the association was weaker than for height (Wang et al. 2011). Similar results were also found in a UK study finding that height was a better predictor of CHD incidence than leg length (Ferrie et al. 2006). On the other hand, in a study of UK 14 years old children, leg length was a better predictor of CHD mortality than height (Gunnell et al. 1998). There is also evidence that not only short leg length but also small leg length-height ratio is associated with increased risk of T2D (Johnston et al. 2013, Conway et al. 2012, Asao et al. 2006). There is thus consistent evidence that leg length is inversely associated with risk of metabolic diseases, and

it may have additional value with total height when predicting T2D. However more original research and a systematic meta-analysis are needed to study which of the components of height is the best predictor of further risk of metabolic diseases. Also more studies on children with sufficiently long follow-up time and measures on leg length and other components of height would be useful to study more detailed how they are associated with further disease risks.

Longitudinal measures

It is very possible that growth trajectories over childhood are more important factors affecting further health risks than body morphology at a certain age. These trajectories would not be captured by the cross-sectional studies discussed above. For example, the theory of biological programming suggests that poor nutrition in fetal life predisposes to further risk of metabolic diseases especially if it is associated with good post-natal environment (Barker 1998). This theory would thus predict that especially rapid catch-up growth over childhood would be associated with increased risk of metabolic diseases since it indicates large improvement in nutrition from pre-natal to post-natal life. Longitudinal studies that can capture the relationships between growth trajectories and future health risks are thus important, because they can give more information on environmental changes. The challenge, however, is that the prolonged periods of time between childhood and adult health outcomes means that such studies are rarer than studies using only cross-sectional measures. Evidence on the association between catch-up growth and increased risk of CVD was found in a Finnish study. This study found that people with hypertension at 63 years of age had lower birth weight and showed catch-up growth in height and weight until 11 years of age when compared to men and women with normal blood pressure (Eriksson et al. 2007). In this same cohort it was also found that CHD incidence was higher in women who had short birth length and who had experienced catch-up growth until 7 years of age (Forsen et al. 1999). So these results seem to support the hypothesis that early catch-up growth associated with low birth weight and short birth length is associated with higher incidence of CVD in adulthood. However, even in these studies it is

difficult to separate the effect of low birth weight and further catch-up growth. As discussed earlier in this chapter, birth weight by itself is associated with the risk of metabolic diseases and it is natural that at least in modern societies with good infant nutrition low birth weight babies experience catch-up growth. Further studies are needed to separate the effects of low birth weight and further catch-up growth on the risk of metabolic diseases.

Catch up growth in mid-childhood may also be associated with future CVD risk. In a Danish study, rapid growth between 7 and 9 years of age was associated with increased CHD incidence in adulthood (Silventoinen et al. 2012a). These results show that even at the time of the slow growth of mid-childhood, growth is associated with CHD risk. However, the strongest association was found between rapid growth from 9 to 11 years in girls and 11 to 13 years in boys. This suggests that especially rapid growth at the onset of puberty, probably indicating early start of puberty, is associated with higher CHD risk. This result is consistent with previous studies finding that early puberty is associated with several risk factors of CHD including hypertension (Hardy et al. 2006) and adverse lipid profile (Feng et al. 2008). In this Danish study the association between height in childhood and further CHD risk was, however, not modified by birth weight (Silventoinen et al. 2012a). So this study did not find evidence that catch-up growth from infancy to mid-childhood was important for CHD risk.

There is thus some evidence that those children who grow faster than their peers have higher risk of CHD in adulthood even when the results are not fully consistent. However, these results should be treated with caution because there are so few epidemiological studies having longitudinal anthropometric measures as compared to those studies having cross-sectional measures. All of these previous studies are based on Nordic populations and represent only two epidemiological cohorts. Replications in other data sets collected in other populations with different environmental exposures would thus be warranted. Especially the role of catch-up growth in infancy as an independent risk factor of CHD needs more research.

General conclusions

In this chapter the role of different anthropometric indicators in the formation of the risk of metabolic diseases was discussed. Childhood physical development is sensitive to environmental factors, especially nutrition, and thus it has attracted scientific interest as anthropometric measures are convenient proxy measures of childhood environmental conditions. Birth weight and length are affected by fetal environment whereas height reflects also environmental conditions over the growth period. Thus the associations between low birth weight and short stature with increased risk of CHD, stroke and T2D suggest that environmental factors during the growth period predisposes to metabolic abnormalities. Overweight in childhood is a strong predictor of obesity in adulthood, and even children with slight overweight have increased risk of CHD in adulthood as compared to lean children. All of these associations demonstrate the importance of early life in the formation of metabolic risk profile affecting health decades later.

In spite of intensive research there are still important gaps in knowledge when considering the associations between childhood anthropometrics and future disease risk. Epidemiological studies need long follow-up time and thus usually have to rely on data sets collected for other than research purposes. Height and weight have been part of health check-up protocol for decades in many countries and can thus be used in epidemiological studies, but much less is known about other anthropometric measures, especially in children. Because the growth velocity of body parts vary at different phases of childhood, it is possible that they also capture different environmental variation. Thus, use of different anthropometric indicators, such as head or chest circumference, may give additional information on the susceptibility periods for the further disease risks. So far the only anthropometric measure widely used in epidemiological studies in addition to height and weight is leg length. There is evidence that leg length can give additional information as compared to height when predicting T2D risk but for CHD the results are somewhat inconsistent. However these results

suggest that the use of other anthropometric indicators would we warranted in further epidemiological studies.

Another area of research where relatively little is known is how developmental trajectories are associated with further disease risks. The reason is that there are only a few big data sets having longitudinal anthropometric measures over childhood and information on disease incidence in adulthood. Studies so far suggest that rapid growth from infancy to the onset of puberty is associated with increased risk of CHD. However, it is still unclear how much of this association is related to low birth weight or early onset of puberty which are both associated with increased risk of metabolic diseases. These studies would be important because they can give more information on the poorly understood physiological pathways between childhood anthropometrics and further disease incidence.

The third large gap of knowledge concerns the associations between childhood anthropometrics and chronic diseases other than metabolic diseases. For example, it is known that tall stature is a risk factor of different cancers both in men and women; thus, the associations of height with risk of cancer is opposite of the risk of metabolic diseases (Wiren et al. 2014). It is noteworthy that height is associated with the increased risk of very different type of cancers, such as melanoma and colon cancer, having otherwise different environmental risk factors. These associations suggest that physical development in childhood is important also for further cancer risk, but very little is known on the physiological pathways behind these associations. Thus this area would warrant further research, preferable with longitudinal measures on physical development in childhood.

In conclusion: epidemiological studies have shown that low birth weight, short stature and short leg length are associated with increased risk of all CVD and T2D. Stature and leg length can also be measured in adulthood, but measures in childhood would be more sensitive for environmental conditions and give better estimates for further disease risk. These associations suggest that inadequate nutrition in early life predisposes to metabolic abnormalities leading to increased disease

risk decades later. However, in industrialized societies and increasingly also in developing countries excess nutrition has replaced under nutrition as a major risk factor for further health. Subsequently relative weight has replaced stature as the most important anthropometric indicator of further risk of metabolic diseases. All of these associations, however, demonstrate the deep roots of adult health in early life and emphasize the need of optimal environment for children to develop as healthy adults.

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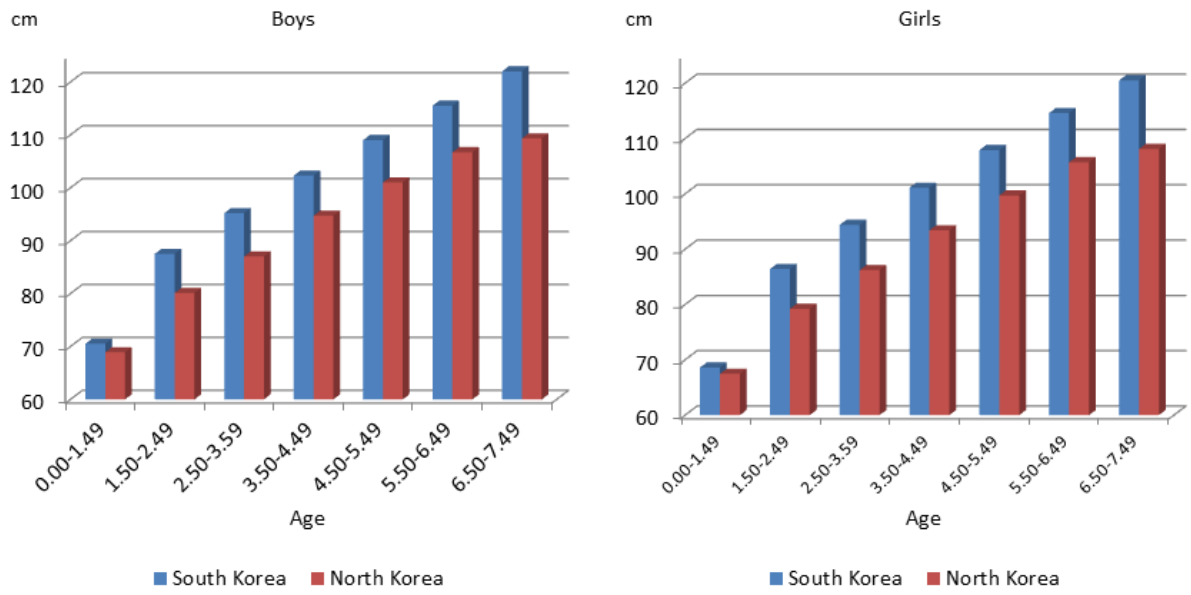
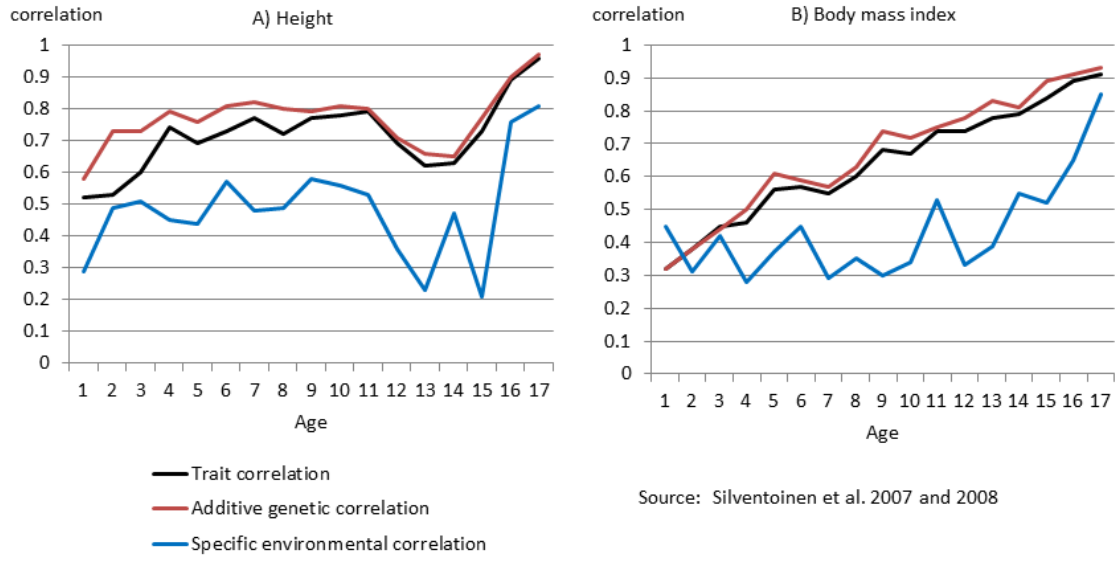
Figure 1. Height in South and North Korean children from birth until seven years of age in 2002/2003.



Source: Schwekendiek, J Biosoc Sci, 2009

Figure 2. Trait correlations and additive genetic and specific environmental correlations of height and body mass index from 1 to 17 years of age with 18 years of age in Swedish twin boys.



Source: Silventoinen et al. 2007 and 2008

Figure 3. Hazard ratios for CHD incidence in adulthood per 1 unit increase in z-scores of height from 7 to 13 years of age in Danish children.